LRPGGKKKYKLKHIVWASRE

```
QUERY                 LRPGGKKKYKLKHIVWASRE

CONSENSUS_A           ---------r---l------
A.KE.Q23-CXC-CG       ---------RM--LI-----
A.SE.SE6594           ---------R---L------
A.SE.SE7253           ---------RM--L------
A.SE.SE7535           -------Q-R---L------
A.SE.SE8131           -----N---R---L------
A.SE.SE8538           ---------RM--L------
A.SE.SE8891           -------------M---R--
A.UG.92UG037          ---------R---L------
A.UG.U455             -----N---R---L------

CONSENSUS_B           --------------------
B.AU.AF128998         -------T-Q----------
B.-.NL43E9            -------L------I-----
B.AU.MBC18            --------------------
B.AU.MBC200           -------Q-R----------
B.AU.MBC925           ---R-----Q----------
B.AU.MBCC54           ---------Q----------
B.AU.MBCC98           ---------Q----------
B.AU.MBCD36           -----R---Q----------
B.CN.RL42             ---------R---L------
B.DE.D31              ---------R----------
B.DE.HAN              ---------Q----------
B.ES.89SP061          ---------R---L------
B.FR.HXB2             --------------------
B.GA.OYI              ---------Q----------
B.GB.CAM1             --------------------
B.GB.MANC             --------------------
B.JP.JH31             --------------------
B.NL.3202A21          -------R------------
B.TW.LM49             ---------R---L------
B.US.85WCIPR54        --------------------
B.US.AD8              --------------------
B.US.BC               -------------L------
B.US.DH123            --------------------
B.US.JRCSF            ---------R----------
B.US.JRFL             ---------R----------
B.US.MNCG             -------------V------
B.US.NC7              ---------M----------
B.US.NY5CG            -------Q-R----------
B.US.P896             --------------------
B.US.RF               ---R---R------------
B.US.SF2              --------------------
B.US.WC001            --------------------
B.US.WEAU160          -----N--------------
B.US.WR27             ---------R---L------
B.US.YU2              -------Q-R----------

CONSENSUS_C           -------h-m---l------
C.BR.92BR025          -K-----H-MM--L------
C.BW.96BW01B22        -------C-M---L------
C.BW.96BW0402         -------Q-RI--L------
C.BW.96BW0502         -------H-M---L------
C.BW.96BW1104         -------R-MI--L------
C.BW.96BW1210         -------R-MM--L------
C.BW.96BW15B03        S------C-M----------
C.BW.96BW1626         -------R-M---L------
C.BW.96BW17A09        -------H-M---L------
C.ET.ETH2220          -------H-M---L---N--
C.IN.93IN904          -------H-M---L------
C.IN.93IN905          -------H-M---L------
C.IN.93IN999          -------H-M---L------
C.IN.94IN11246        -------H-M---L------
C.IN.95IN21068        -------R-M---L------

CONSENSUS_D           ---------r---l------
D.CD.84ZR085          --------------------
D.CD.ELI              ---------R----------
D.CD.NDK              ---------A---LI-----
D.CD.Z2Z6             ---------R---L------
D.UG.94UG1141         ---------R---L------

CONSENSUS_F           ---------rm--L------
F.BR.BZ162            ---------R---L------
F.CD.VI174            ---------RM--L------
F.RW.VI69             -----R----M--LI-----

CONSENSUS_F1          ---------rm--L------
F1.BE.VI850           -------R--M--LI-----
F1.BR.93BR020.1       ---------R---L------
F1.FI.FIN9363         -------Q-RI--L------
F1.FR.MP411           ---------RM--L------

CONSENSUS_F2          -?-----?-R---?------
F2.CM.MP255           -K-----R-R---L------
F2.CM.MP257           ---------R----------

CONSENSUS_G           -----x---xx--L------
G.BE.DRCBL            -------R-RM--L------
G.FI.HH8793           ---------R---L------
G.NG.92NG083          -----R--------------
G.SE.SE6165           -----R-S--I--L------

CONSENSUS_H           ---------R---L------
H.BE.VI991            -----R---R---L------
H.BE.VI997            ---------R----------
H.CF.90CF056          ---------R---L------

CONSENSUS_J           -------?-RI--L------
J.SE.SE9173           -------Q-RI--L------
J.SE.SE9280           ---------RI--L------

CONSENSUS_K           ---------r---L------
K.BE.VI325            -----S---R---L------
K.CD.EQTB11C          ---------R---L------
K.CM.MP535            -------------L------
N.CM.YBF30            ---------RM--L------

CONSENSUS_O           -?--S--?-R---L------
O.CM.ANT70C           -K--S----R---L------
O.CM.MVP5180          ----S--A-R---L------
CRF01-AE.CF.90CF40    -------Q-RM--L------
CRF01-AE.TH.93TH25    ----------M--L------
CRF01-AE.TH.CM240     -----R---R---L------
CRF01-AE.TH.TH022     -----R---RM--L------
CRF01-AE.TH.TH047     -----R---H----------
CRF02_AG.FR.DJ263     ---------R---L------
CRF02_AG.FR.DJ264     ---A-----R---L------
CRF02_AG.NG.IBNG      ---------R---L------
CRF03_AB.RU.KAL15     ------E--RI--L------
CRF04_cpx.CY.94CY0    ---------R---L------
CRF04_cpx.GR.97PVC    ---------R---L------
CRF04_cpx.GR.97PVM    -------R-RI--LI-----
AC.ET.E3099G          -----N---R---L------
AC.IN.21301           -------H-MI--L------
AC.RW.92RW009         -K-----T-MM--L------
AC.SE.SE9488          ---------RM--L------
AC.ZM.ZAM174-21       -----S-R-MI--L------
AC.ZM.ZAM184          -------Q-RM--L------
AC.ZM.ZAM716-17       -------Q-RI--L------
ACD.SE.SE8603         ---------R---L------
AD.SE.SE6954          -------R-R----------
AD.SE.SE7108          -----R--------------
ADHU.NO.NOGIL3        -------Q-R---L------
ADU.CD.MAL            ---------R---L------
AG.NG.G3              ---------RM--L------
AG.SE.SE7812          ---------R---L------
AGHU.GA.VI354         ---------QI---------
AGJ.AU.BFP90          ----------M--L------
AGJ.ML.95ML8          ---------RM--L------
AGU.CD.Z321           -------Q------------
BF.BR.93BR029.4       -----H---R----------
DF.CD.VI961           ---------R----------
U.CD.VI1126           -----R---R---L------

CONSENSUS_CPZ         ---------Mm--L------
CPZ.CD.CPZANT         ---------MI--L---RS-
CPZ.GA.CPZGAB         -----R-R-MM--L------
CPZ.US.CPZUS          ---------MM--L------
```

EKASFPEVIPMFSALSEGAT

QUERY	**EKASFPEVIPMFSALSEGAT**
CONSENSUS_A	---fs---------------
A.KE.Q23-CXC-CG	---FS---------------
A.SE.SE6594	--GFN---------------
A.SE.SE7253	---FS-----V---------
A.SE.SE7535	---FS---------------
A.SE.SE8131	-R-FS---------------
A.SE.SE8538	--GFN---------------
A.SE.SE8891	--GFS---------------
A.UG.92UG037	---LS---------------
A.UG.U455	D--FS---------------
CONSENSUS_B	---FS---------------
B.AU.AF128998	---FS---------------
B.-.NL43E9	---FS---------------
B.AU.MBC18	---FS---------------
B.AU.MBC200	---FS---------------
B.AU.MBC925	---FS---------------
B.AU.MBCC54	---FS---------------
B.AU.MBCC98	---FS---------------
B.AU.MBCD36	---FS-------T-------
B.CN.RL42	---FS---------------
B.DE.D31	---FS---------------
B.DE.HAN	---FS---------------
B.ES.89SP061	---FS---------------
B.FR.HXB2	---FS---------------
B.GA.OYI	---FS----------A----
B.GB.CAM1	---FS---------------
B.GB.MANC	---FS--------------I
B.JP.JH31	---FS---------------
B.NL.3202A21	---FS---------------
B.TW.LM49	---FS---------------
B.US.85WCIPR54	---FS---------------
B.US.AD8	---FS---------------
B.US.BC	---FS---------------
B.US.DH123	---FS---------------
B.US.JRCSF	---FS---------------
B.US.JRFL	---FS---------------
B.US.MNCG	---FS---------------
B.US.NC7	---FS---------------
B.US.NY5CG	---FS---------------
B.US.P896	---FS---------------
B.US.RF	---FS---------------
B.US.SF2	---FS---------------
B.US.WC001	---FS---------------
B.US.WEAU160	---FS---------------
B.US.WR27	---FS---------------
B.US.YU2	---FS---------------
CONSENSUS_C	---FS-------T-------
C.BR.92BR025	---FS-------T-------
C.BW.96BW01B22	---FS-------T-------
C.BW.96BW0402	---FS-------T-------
C.BW.96BW0502	---FS-------T-------
C.BW.96BW1104	---FS-------T-------
C.BW.96BW1210	---FS--I----T-------
C.BW.96BW15B03	---FS-------T-------
C.BW.96BW1626	---FS-------T-------
C.BW.96BW17A09	---FS-------T-------
C.ET.ETH2220	---FS-------T-------
C.IN.93IN904	---FS-------T-------
C.IN.93IN905	---FS-------T-------
C.IN.93IN999	---FS-------T-------
C.IN.94IN11246	---FS-------T-------
C.IN.95IN21068	---FS-------T-------
CONSENSUS_D	---Fs---------------
D.CD.84ZR085	---FN---------------
D.CD.ELI	---FS---------------
D.CD.NDK	---FS---------------
D.CD.Z2Z6	---FS---------------
D.UG.94UG1141	---FN---------------
CONSENSUS_F	---FS---------------
F.BR.BZ162	---FS---------------
F.CD.VI174	---FS---------------
F.RW.VI69	---FS---------------
CONSENSUS_F1	---FS---------------
F1.BE.VI850	---FS---------------
F1.BR.93BR020.1	---FS---------------
F1.FI.FIN9363	---FS---------------
F1.FR.MP411	---FS---------------
CONSENSUS_F2	---FS---------------
F2.CM.MP255	---FS---------------
F2.CM.MP257	---FS---------------
CONSENSUS_G	---FS---------------
G.BE.DRCBL	---FS-------T-------
G.FI.HH8793	---FS---------------
G.NG.92NG083	---FS---------------
G.SE.SE6165	---FS---------------
CONSENSUS_H	---FS---------------
H.BE.VI991	---FS---------------
H.BE.VI997	---FS---------------
H.CF.90CF056	---FS---------------
CONSENSUS_J	---FS---------------
J.SE.SE9173	---FS---------------
J.SE.SE9280	---FS---------------
CONSENSUS_K	---FS---------------
K.BE.VI325	---FS----------AD---
K.CD.EQTB11C	---FS---------------
K.CM.MP535	---FS-------T-------
N.CM.YBF30	---FS-------M-------
CONSENSUS_O	---FN--I----M------?
O.CM.ANT70C	---FN--I----M------I
O.CM.MVP5180	---FN--I----M------V
CRF01-AE.CF.90CF40	--GFN---------------
CRF01-AE.TH.93TH25	--GFN---------------
CRF01-AE.TH.CM240	--GFN---------------
CRF01-AE.TH.TH022	--GFN---------------
CRF01-AE.TH.TH047	--GFS---------------
CRF02_AG.FR.DJ263	---FS-------T-------
CRF02_AG.FR.DJ264	---FS-------T-------
CRF02_AG.NG.IBNG	--GFS---------------
CRF03_AB.RU.KAL15	---FS---------------
CRF04_cpx.CY.94CY0	---FS---------------
CRF04_cpx.GR.97PVC	---FS---------------
CRF04_cpx.GR.97PVM	--GFS---------------
AC.ET.E3099G	---FS---------------
AC.IN.21301	---FS--I----T-------
AC.RW.92RW009	---FSQ------T-------
AC.SE.SE9488	D--FS-------T-------
AC.ZM.ZAM174-21	---FS-------T-------
AC.ZM.ZAM184	---FS---------------
AC.ZM.ZAM716-17	---FS-------T-------
ACD.SE.SE8603	---FS---------------
AD.SE.SE6954	---FS--------------A
AD.SE.SE7108	---FS---------------
ADHU.NO.NOGIL3	---FS-----------D---
ADU.CD.MAL	---FS---------------
AG.NG.G3	--NFS-------T-------
AG.SE.SE7812	---FS---------------
AGHU.GA.VI354	--GFS---------------
AGJ.AU.BFP90	D--FS-------T-------
AGJ.ML.95ML8	---FS---------------
AGU.CD.Z321	--NFS---------------
BF.BR.93BR029.4	---FS---------------
DF.CD.VI961	---FS-------T-------
U.CD.VI1126	---FS-------T-------
CONSENSUS_CPZ	---Fn---------------
CPZ.CD.CPZANT	--NFN---------------
CPZ.GA.CPZGAB	---FS--------------L
CPZ.US.CPZUS	---FN-------M-------

Study Subject ID:00RCH59
Study Subject Clone:
Study Subject HLA:A34,A74,B8,B57,Cw10,Cw7
Sequence: Known reactive 20Mer0: LRPGGKKKYKLKHIVWASRE p17(21–40)

Possible HLA

A34	A*3401,A*3402
A74	A*7401,A*7402
B57	Bw57,B*57,B*5701,B*5702,B*5703,B*5704
B8	B*0801,B*0802,B*0803,B*0806
Cw10	Cw*0302,Cw*0304
Cw7	Cw*0701,Cw*0702,Cw*0704,Cw*0706

Possible Epitopes based on anchor residues

(4-11)	GGKKKYKL	B8
(1-9)	LRPGGKKKY	Cw*0702
(3-11)	PGGKKKYKL	Cw*0702
(2-9)	RPGGKKKY	Cw*0702
(4-11)	GGKKKYKL	Cw*0702
(2-11)	RPGGKKKYKL	Cw*0702

Anchor Residues Searched

B8	XX[K]X[KR]XXX[L]
B8	XX[K]X[KR]XX[L]
B8	XX[K]X[KR]XXXX[L]
Cw*0304	X[A]XXXXXX[LM]
Cw*0304	X[A]XXXXX[LM]
Cw*0304	X[A]XXXXXXX[LM]
Cw*0702	XXXXXXXX[YFL]
Cw*0702	XXXXXXX[YFL]
Cw*0702	XXXXXXXXX[YFL]

Study Subject ID:00RCH59
Study Subject Clone:
Study Subject HLA:A34,A74,B8,B57,Cw10,Cw7
Sequence: Known reactive 20Mer1: EKASFPEVIPMFSALSEGAT p24(29–48)

Possible HLA

A34	A*3401,A*3402
A74	A*7401,A*7402
B57	Bw57,B*57,B*5701,B*5702,B*5703,B*5704
B8	B*0801,B*0802,B*0803,B*0806
Cw10	Cw*0302,Cw*0304
Cw7	Cw*0701,Cw*0702,Cw*0704,Cw*0706

Possible Epitopes based on anchor residues

(2-11)	KASFPEVIPM	Cw*0304
(4-12)	SFPEVIPMF	Cw*0702
(7-15)	EVIPMFSAL	Cw*0702
(5-12)	FPEVIPMF	Cw*0702
(8-15)	VIPMFSAL	Cw*0702
(3-12)	ASFPEVIPMF	Cw*0702
(6-15)	PEVIPMFSAL	Cw*0702

Anchor Residues Searched

B8	XX[K]X[KR]XXX[L]
B8	XX[K]X[KR]XX[L]
B8	XX[K]X[KR]XXXX[L]
Cw*0304	X[A]XXXXXX[LM]
Cw*0304	X[A]XXXXX[LM]
Cw*0304	X[A]XXXXXXX[LM]
Cw*0702	XXXXXXXX[YFL]
Cw*0702	XXXXXXX[YFL]
Cw*0702	XXXXXXXXX[YFL]

This table lists epitopes that are experimentally observed to be presented by a HLA type carried by the patient, but the de£ned epitope has substitutions relative to the peptides from your reference strains and so might be missed by your reagents: in HXB2 for Gag, Pol; MN for Env; BRU for Nef, relative to most B clade Sequences in the database:

Protein	Epitope in Database	Epitope in Ref. strain	Epitope in Consensus B	HLA	Notes
p24(15–23)	LSPRTLNAW	ISPRTLNAW	ISPRTLNAW	B57,B58	
p24(108–117)	TSTLQEQIGWF	TSTLQEQIGWM	TSTLQEQIGWM	B*57,B*5801	
p24(108–118)	TSTLQEQIGWF	TSTLQEQIGWM	TSTLQEQIGWM	B*5701	
p24(127–135)	GDIYKRWII	GEIYKRWII	GEIYKRWII	B*0801	
p24(128–135)	DIYKRWII	EIYKRWII	EIYKRWII	B8	
Protease(3–11)	ITLWQRPLV	VTLWQRPLV	ITLWQRPLV	A*6802,A*7401,A19	
Protease(3–11)	ITLWQRPLV	VTLWQRPLV	ITLWQRPLV	A*7401	
gp160(2–10)	RVKEKYQHL	RAIEAQQHM	GIRKNYQHL	B*0801	
gp160(2–10)	RVKEKYQHL	RAIEAQQHM	GIRKNYQHL	B8	

Table 1: **p24**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p24(15–23)	p24()	LSPRTLNAW	HIV-1 exposed seronegative	human(B57,B58)	[Kaul (2000)]
	• 11/16 heavily HIV exposed but persistently seronegative sex-workers in Nairobi had HIV-speci£c CD8 gamma-IFN responses in the cervix – systemic CD8+ T cell responses tended to be to the same epitopes but at generally lower levels than cervical CD8+ T cell responses • Low risk individuals did not have such CD8+ cells • CD8+ epitopes T cell DTVLEDINL (3 individuals), SLYNVATL (4 individuals), LSPRTLNAW (3 individuals) and YPLTFGWCF (4 individuals) were most commonly recognized by the HIV-resistant women				
p24(108–117)	p24(240–249 LAI)	TSTLQEQIGWF	HIV-1 infection	human(B*57,B*5801)	[Goulder (1996)]
	• Response to this epitope was found in 4 slow progressing HLA-B*57 individuals, in 2 it was dominant or very strong • For one donor (from Zimbabwe) this was de£ned as the optimal peptide • This epitope can be presented in the context of the closely related HLA molecules B*5801 and B*57				
p24(108–118)	p24(240–249 LAI)	TSTLQEQIGWF	HIV-1 infection	human(B*5701)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*5701 epitope				
p24(127–135)	p24(259–267 SF2)	GDIYKRWII	HIV-1 infection	human(B*0801)	[McAdam (1998)]
	• GDIYKRWII speci£c CTL clone also recognized GEIYKRWII				
p24(128–135)	p24()	DIYKRWII	HIV-1 infection	human(B8)	[Goulder (2000)]
	• The CTL-dominant response was focused on this epitope in a HIV+ South African – this epitope did not fall within the £ve most recognized peptides in the study • Three peptides GSEELRSLYNTVATL (p17 residues 71-85), SALSEGATPQDLNTMLNTVG (p24 41-60), and WEKIRLRPG-GKKKYKLK(p17 16-30) contained the dominant Gag-speci£c epitope in 31 out of 44 B-clade infected individuals from Boston who showed Gag-CTL responses • Five peptides RLRPGGKKHYMIKHLVW (p17 20-36), ELRSLYNTVATLYCV (p17Gag 74-88), SALSEGATPQDLNTMLNTVG (p24 41-60), FRDYVDRFFKTLRAEQA (p24 161-177), and SILDIKQGKEPFRDY (p24 149-164) contained dominant Gag-speci£c epitopes in 32 out of 37 C-clade infected subjects from South Africa				

Table 2: **Protease**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
Protease(3–11)	Protease(71–79 LAI)	ITLWQRPLV		human(A*6802,A*7401,A19)	[Dong (1998)]
	• Predicted on binding motif, no truncations analyzed • Clade A/B/D consensus, S. Rowland-Jones, pers. comm.				
Protease(3–11)	RT(71–79 A/B/D)	ITLWQRPLV	?	human(A*7401)	[Brander & Goulder(2001)]
	• C. Brander notes this is an A*7401 epitope				

Table 3: **gp160**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
gp160(2–10)	gp160(2–10 IIIB)	RVKEKYQHL	HIV-1 infection	human(B*0801)	[Brander & Goulder(2001)]
	• C. Brander notes this is a B*0801 epitope				
gp160(2–10)	gp160(2–10 IIIB)	RVKEKYQHL	HIV-1 infection	human(B8)	[Sipsas (1997)]
	• HIV IIIB proteins were used to de£ne the range of CTL epitopes recognized by 3 lab workers accidentally infected with HIV-1 IIIB • Type-speci£c epitope, unique to the LAI and IIIB because of a deletion of three amino acids that are present in all other subtype B HIV-1s • RVKGIRKNYQHL, a variant found in JRCSF, was not recognized • This epitope is in the signal sequence of gp120				

Table 4: All De£ned Epitopes within the 20mer, regardless of HLA type

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(21–35)	Gag()	LRPGGKKKYKLKHIV	HIV-infection	human()	[Weekes (1999a)]
	• Peptide 703.3: Memory CTL speci£c for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations				
p17(21–35)	p17(91–105 SF2)	LRPGGKKKYKLKHIV	HIV-1 infection	human()	[Lieberman (1997)]
	• Of 25 patients, most had CTL speci£c for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A1, A2, B50, B57				
p17(21–35)	Gag()	LRPGGKKKYKLKHIV	HIV-infection	human(A3)	[Weekes (1999b)]
	• Peptide 703.3: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones speci£c for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population • HIV CTL responses to 3 Env and 2 Gag peptides were studied • The clonal composition of the TCR Vbeta responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-speci£c response – clones to this epitope were Vbeta13.1 and Vbeta5.2				
p17(21–35)	p17(21–35)	LRPGGKKKYKLKHIV		human(B8)	[Nixon & McMichael(1991)]
	• Two CTL epitopes de£ned (see also p24(191-205))				
p17(21–35)	p17(21–35)	LRPGGKKKYKLKHIV	HIV-1 infection	human(not B8)	[van Baalen (1996)]
	• Unknown HLA speci£city, but not B8				
p17(21–40)	p17(21–40 Clade A)	LRPGGKKKYRLKHLVWASRE	HIV-1 infection	human(Cw4)	[Dorrell (1999)]
	• CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa • This epitope was de£ned in an A subtype infection – the B clade variant (LRPGGKKKYKLKHIVWASRE) has two mutations relative to the A subtype form, and the CTL from this patient were not A-B cross-reactive				
p17(22–31)	Gag(22–31)	RPGGKKRYKL	HIV-1 infection	human(B7)	[Jin (2000)]
	• This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor • A dominant B7 epitope was de£ned using conventional methods, and three additional sub-dominant HLA B7 epitopes were de£ned by £rst using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–31)	p17(24–31)	GGKKKYKL		human(B8)	[Goulder (1997b)]

- The crystal structure of this peptide bound to HLA-B8 was used to predict new epitopes and the consequences of epitope variation
- The predictions were experimentally con£rmed
- The anchors for HLA-B8 epitopes, as de£ned by peptide elution data, are P3 (K), P5 (K/R), and P8 (L)
- Structural data suggests that a positive charge at P5 is essential, but that the constraints on P3 may be less severe
- Small hydrophobic residues at P2 may be favorable for binding
- A spacious F-pocket favors mid-sized hydrophobic residues in the C-term anchor

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–31)	p17(24–31 SF2)	GGKKKYKL	HIV-1 infection	human(B8)	[McAdam (1998)]

- CTL from a patient infected with clade B virus did not recognize Ugandan variants of this epitope

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–31)	p17(24–31 LAI)	GGKKKYKL	HIV-1 infection	human(B8)	[Reid (1996)]

- The variants 7R: GGKKKYRL, 7Q: GGKKKYQL, 5R: GGKKRYKL, and 3R: GGRKKYKL, were studied
- Crystal structures were obtained to study these peptides in the context of HLA-B8, and CTL binding and activity were determined
- 3R has been detected in 3 patients, and it abolishes recognition causing extensive conformational changes upon binding including MHC main chain movement
- 7Q and 7R alter the TCR exposed surface, and retain some recognition
- Reactivity of 5R depends on the T cell clone, this amino acid is embedded in the C pocket of B8 when the peptide is bound
- Optimal peptide is 8-mer, not 9-mer, and positions 3, 5, and 8 are the anchor residues

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–31)	p17(24–31 LAI)	GGKKKYKL	HIV-1 infection	human(B8)	[Price (1997)]

- A weak CTL response to the index peptide was observed in an HLA-B8+ infected individual
- Sequences from the earliest available time point showed that a variant at position 5, an anchor residue, GGKKQYKL, was present

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B*0801)	[Brander & Goulder(2001)]

- C. Brander notes epitope to be presented by B*0801

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B8)	[Sutton (1993)]

- Exploration of HLA-B8 binding motif through peptide elution

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B8)	[Rowland-Jones (1993)]

- Study of an individual with partially defective antigen processing

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Klenerman (1994)]

- Naturally occurring variants GGKKKYQLK and GGKKRYRLK may act as antagonists

p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Klenerman (1995)]

- Naturally occurring antagonist GGKKKYQLK found in viral PBMC DNA and RNA

p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Nowak (1995)]

- Longitudinal study of CTL response and immune escape – the variant GGRKKYKLK binds to HLA-B8 but is not reactive

p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Dyer (1999)]

- CTL speci£c responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective
- Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load

p17(24–32)	p17()	GGKKKYKLK		human(B8)	[Rowland-Jones (1999)]

- CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5
- In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective
- HIV-2 sequence: GGKKKYKMK – no cross-reactivity [Phillips (1991)]

p17(24–35)	p17(25–35 SF2)	GGKKKYKLKHIV	HIV-1 infection	human(B8)	[Phillips (1991), Goulder (1997a)]

- Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time
- [Goulder (1997a)] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients

p17(24–35)	p17(25–35)	GGKKKYKLKHIV	HIV-1 infection	human(B8)	[Birk (1998)]

- A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is in¤uenced by immune pressure from CTLs

p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A*2402)	[Brander & Goulder(2001)]

- Ikeda-Moore(1998) and D. Lewinsohn, pers. comm.
- C. Brander notes that this is an A*2402 epitope

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(28–36)	p17(28–36 SF2)	KYKLKHIVW	HIV-1 infection	human(A*2402)	[Ikeda-Moore (1998)]

- Strong CTL activity to this peptide was detected in 2/3 HIV-infected individuals who were HLA A24+
- HLA A24 is very common in Japanese (70% carry it) and is common globally
- This epitope was detected by looking for peptides with appropriate A24 anchor residues (Y at position 2, carb-term ILF or W) – 16/17 such peptides bound to A24 – KYKLKHIVW was found to be a naturally processed epitope that elicits a strong CTL response.

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A23)	[Goulder & Walker(1999)]

- P. Goulder, pers. comm.

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A24)	[Brander & Walker(1996)]

- D. Lewinsohn, pers. comm.

Table 5: **All De£ned Epitopes within the 20mer, regardless of HLA type**

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(21–35)	Gag()	LRPGGKKKYKLKHIV	HIV-infection	human()	[Weekes (1999a)]
	• Peptide 703.3: Memory CTL speci£c for HIV-1 may contribute to oligoclonal expansions within the CD57+ CD28- CD8+ CTLp populations				
p17(21–35)	p17(91–105 SF2)	LRPGGKKKYKLKHIV	HIV-1 infection	human()	[Lieberman (1997)]
	• Of 25 patients, most had CTL speci£c for more than 1 HIV-1 protein • Twelve subjects had CTL that could recognize vaccinia-expressed LAI gag • One of these 12 had CTL response to this peptide • The responding subject was HLA-A1, A2, B50, B57				
p17(21–35)	Gag()	LRPGGKKKYKLKHIV	HIV-infection	human(A3)	[Weekes (1999b)]
	• Peptide 703.3: Almost all CD8+ T cells are CD28+ at birth, and the proportion of CD28-CD8+ cells increases with age – this study examines the contribution of CD8+CD28- cells to CTL memory pools for CTL clones speci£c for two persistent human viruses, CMV and HIV – clones were found to be similarly distributed in the CD28 depleted cell population • HIV CTL responses to 3 Env and 2 Gag peptides were studied • The clonal composition of the TCR Vbeta responses was studied and was found to be highly focused, with one TCR beta-chain sequence tending to dominate the peptide-speci£c response – clones to this epitope were Vbeta13.1 and Vbeta5.2				
p17(21–35)	p17(21–35)	LRPGGKKKYKLKHIV		human(B8)	[Nixon & McMichael(1991)]
	• Two CTL epitopes de£ned (see also p24(191-205))				
p17(21–35)	p17(21–35)	LRPGGKKKYKLKHIV	HIV-1 infection	human(not B8)	[van Baalen (1996)]
	• Unknown HLA speci£city, but not B8				
p17(21–40)	p17(21–40 Clade A)	LRPGGKKKYRLKHLVWASRE	HIV-1 infection	human(Cw4)	[Dorrell (1999)]
	• CTL responses in three individuals with non-clade B infections were studied, 2 with subtype A infections, 1 with subtype C – their infections all originated in East Africa • This epitope was de£ned in an A subtype infection – the B clade variant (LRPGGKKKYKLKHIVWASRE) has two mutations relative to the A subtype form, and the CTL from this patient were not A-B cross-reactive				
p17(22–31)	Gag(22–31)	RPGGKKRYKL	HIV-1 infection	human(B7)	[Jin (2000)]
	• This B7 epitope is one of three subdominant CTL responses detected in a long-term non-progressor • A dominant B7 epitope was de£ned using conventional methods, and three additional sub-dominant HLA B7 epitopes were de£ned by £rst using a non-anchor based strategy, EpiMatrix, to identify 2078 possible epitopes in the autologous HIV-1, followed by B7 anchor residue prediction to narrow the set to 55 peptides for experimental testing				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–31)	p17(24–31)	GGKKKYKL		human(B8)	[Goulder (1997b)]

- The crystal structure of this peptide bound to HLA-B8 was used to predict new epitopes and the consequences of epitope variation
- The predictions were experimentally con£rmed
- The anchors for HLA-B8 epitopes, as de£ned by peptide elution data, are P3 (K), P5 (K/R), and P8 (L)
- Structural data suggests that a positive charge at P5 is essential, but that the constraints on P3 may be less severe
- Small hydrophobic residues at P2 may be favorable for binding
- A spacious F-pocket favors mid-sized hydrophobic residues in the C-term anchor

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–31)	p17(24–31 SF2)	GGKKKYKL	HIV-1 infection	human(B8)	[McAdam (1998)]

- CTL from a patient infected with clade B virus did not recognize Ugandan variants of this epitope

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–31)	p17(24–31 LAI)	GGKKKYKL	HIV-1 infection	human(B8)	[Reid (1996)]

- The variants 7R: GGKKKYRL, 7Q: GGKKKYQL, 5R: GGKKRYKL, and 3R: GGRKKYKL, were studied
- Crystal structures were obtained to study these peptides in the context of HLA-B8, and CTL binding and activity were determined
- 3R has been detected in 3 patients, and it abolishes recognition causing extensive conformational changes upon binding including MHC main chain movement
- 7Q and 7R alter the TCR exposed surface, and retain some recognition
- Reactivity of 5R depends on the T cell clone, this amino acid is embedded in the C pocket of B8 when the peptide is bound
- Optimal peptide is 8-mer, not 9-mer, and positions 3, 5, and 8 are the anchor residues

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–31)	p17(24–31 LAI)	GGKKKYKL	HIV-1 infection	human(B8)	[Price (1997)]

- A weak CTL response to the index peptide was observed in an HLA-B8+ infected individual
- Sequences from the earliest available time point showed that a variant at position 5, an anchor residue, GGKKQYKL, was present

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B*0801)	[Brander & Goulder(2001)]

- C. Brander notes epitope to be presented by B*0801

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B8)	[Sutton (1993)]

- Exploration of HLA-B8 binding motif through peptide elution

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–32)	p17(24–32 LAI)	GGKKKYKLK	HIV-1 infection	human(B8)	[Rowland-Jones (1993)]

- Study of an individual with partially defective antigen processing

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Klenerman (1994)]
	• Naturally occurring variants GGKKKYQLK and GGKKRYRLK may act as antagonists				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Klenerman (1995)]
	• Naturally occurring antagonist GGKKKYQLK found in viral PBMC DNA and RNA				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Nowak (1995)]
	• Longitudinal study of CTL response and immune escape – the variant GGRKKYKLK binds to HLA-B8 but is not reactive				
p17(24–32)	p17(24–32)	GGKKKYKLK	HIV-1 infection	human(B8)	[Dyer (1999)]
	• CTL speci£c responses were measured over a 1.3 to 1.5 year period in members of the Sydney Blood Bank Cohort (SBBC) who had been infected with a natural attenuated strain of HIV-1 which was Nef-defective • Some of these patients had prolonged high levels of CTL effector and memory cells despite low viral load				
p17(24–32)	p17()	GGKKKYKLK		human(B8)	[Rowland-Jones (1999)]
	• CTL responses in seronegative highly HIV-exposed African female sex workers in Gambia and Nairobi were studied – these women had no delta 32 deletion in CCR5 • In Gambia there is exposure to both HIV-1 and HIV-2, CTL responses to B35 epitopes in exposed, uninfected women are cross-reactive, and the B35 allele seems to be protective • HIV-2 sequence: GGKKKYKMK – no cross-reactivity [Phillips (1991)]				
p17(24–35)	p17(25–35 SF2)	GGKKKYKLKHIV	HIV-1 infection	human(B8)	[Phillips (1991), Goulder (1997a)]
	• Longitudinal study of CTL escape mutants in people with the appropriate HLA types – little variation was observed in the immunodominant B27 epitope, relative to B8 epitopes, which varied over time • [Goulder (1997a)] is a review of immune escape that points out that there may be a protective effect associated with B27, and that HLA-B8 individuals tend to progress more rapidly than HLA B27 patients				
p17(24–35)	p17(25–35)	GGKKKYKLKHIV	HIV-1 infection	human(B8)	[Birk (1998)]
	• A study of p17 variation considering known p17 epitopes and individuals with known HLA types revealed that p17 evolution is in¤uenced by immune pressure from CTLs				
p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A*2402)	[Brander & Goulder(2001)]
	• Ikeda-Moore(1998) and D. Lewinsohn, pers. comm. • C. Brander notes that this is an A*2402 epitope				

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
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- Strong CTL activity to this peptide was detected in 2/3 HIV-infected individuals who were HLA A24+
- HLA A24 is very common in Japanese (70% carry it) and is common globally
- This epitope was detected by looking for peptides with appropriate A24 anchor residues (Y at position 2, carb-term ILF or W) – 16/17 such peptides bound to A24 – KYKLKHIVW was found to be a naturally processed epitope that elicits a strong CTL response.

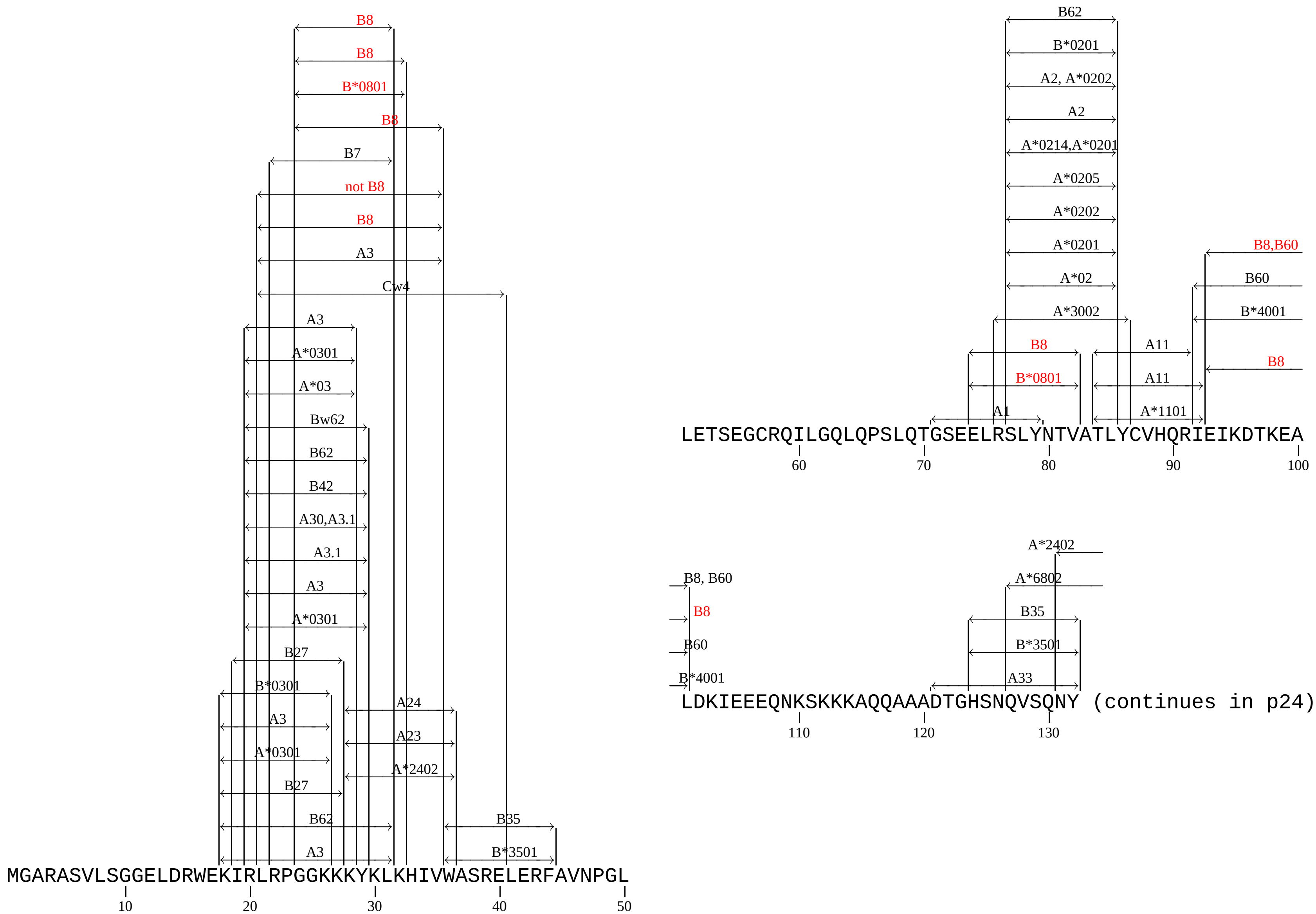
HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A23)	[Goulder & Walker(1999)]

- P. Goulder, pers. comm.

HXB2 Location	Author Location	Sequence	Immunogen	Species(HLA)	References
p17(28–36)	p17(28–36 LAI)	KYKLKHIVW		human(A24)	[Brander & Walker(1996)]

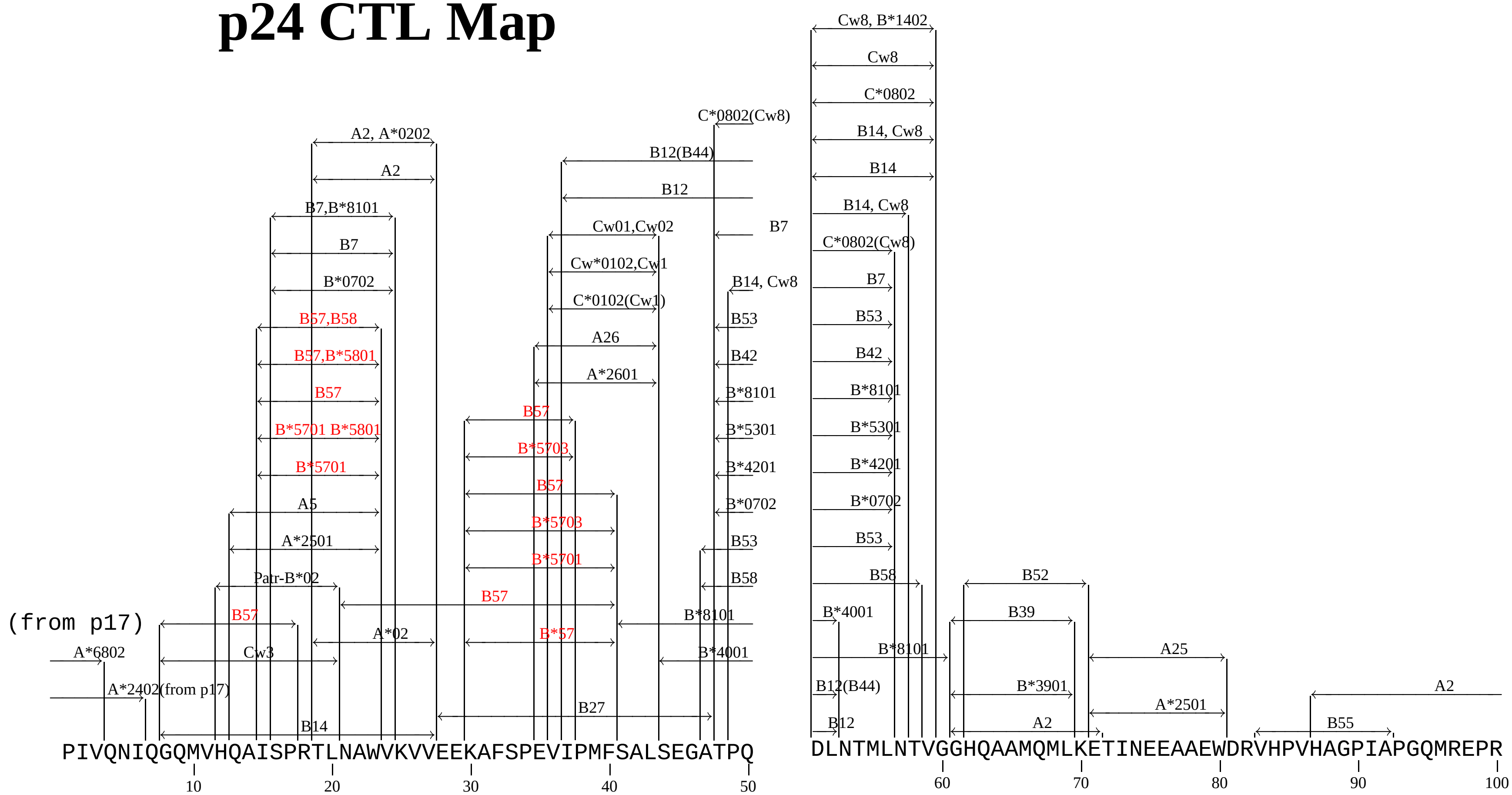
- D. Lewinsohn, pers. comm.

p17 CTL Map



B8
B8
B*0801
B8
B7
not B8
B8
A3
Cw4
A3
A*0301
A*03
Bw62
B62
B42
A30,A3.1
A3.1
A3
A*0301
B27
B*0301
A24
A3
A23
A*0301
A*2402
B27
B62
B35
A3
B*3501
MGARASVLSGGELDRWEKIRLRPGGKKKYKLKHIVWASRELERFAVNPGL
10
20
30
40
50
B62
B*0201
A2, A*0202
A2
A*0214,A*0201
A*0205
A*0202
A*0201
B8,B60
A*02
B60
A*3002
B*4001
B8
A11
B8
B*0801
A11
A1
A*1101
LETSEGCRQILGQLQPSLQTGSEELRSLYNTVATLYCVHQRIEIKDTKEA
60
70
80
90
100
A*2402
B8, B60
A*6802
B8
B35
B60
B*3501
B*4001
A33
LDKIEEEQNKSKKKAQQAAADTGHSNQVSQNY (continues in p24)
110
120
130

p24 CTL Map



(from p17)
A*6802
A*2402(from p17)
B57
Cw3
B14
Patr-B*02
A*2501
A5
B*5701
B*5701 B*5801
B57
B57,B*5801
B57,B58
B*0702
B7
B7,B*8101
A2
A2, A*0202
A*02
B57
B57
B*5703
B57
B*5703
B*5701
B*57
B27
A*2601
A26
C*0102(Cw1)
Cw*0102,Cw1
Cw01,Cw02
B12
B12(B44)
C*0802(Cw8)
B7
B14, Cw8
B53
B42
B*8101
B*5301
B*4201
B*0702
B53
B58
B*8101
B*4001
PIVQNIQGQMVHQAISPRTLNAWVKVVEEKAFSPEVIPMFSALSEGATPQ
10
20
30
40
50
Cw8, B*1402
Cw8
C*0802
B14, Cw8
B14
B14, Cw8
C*0802(Cw8)
B7
B53
B42
B*8101
B*5301
B*4201
B*0702
B53
B58
B*4001
B*8101
B12(B44)
B12
B52
B39
B*3901
A2
A25
A*2501
A2
B55
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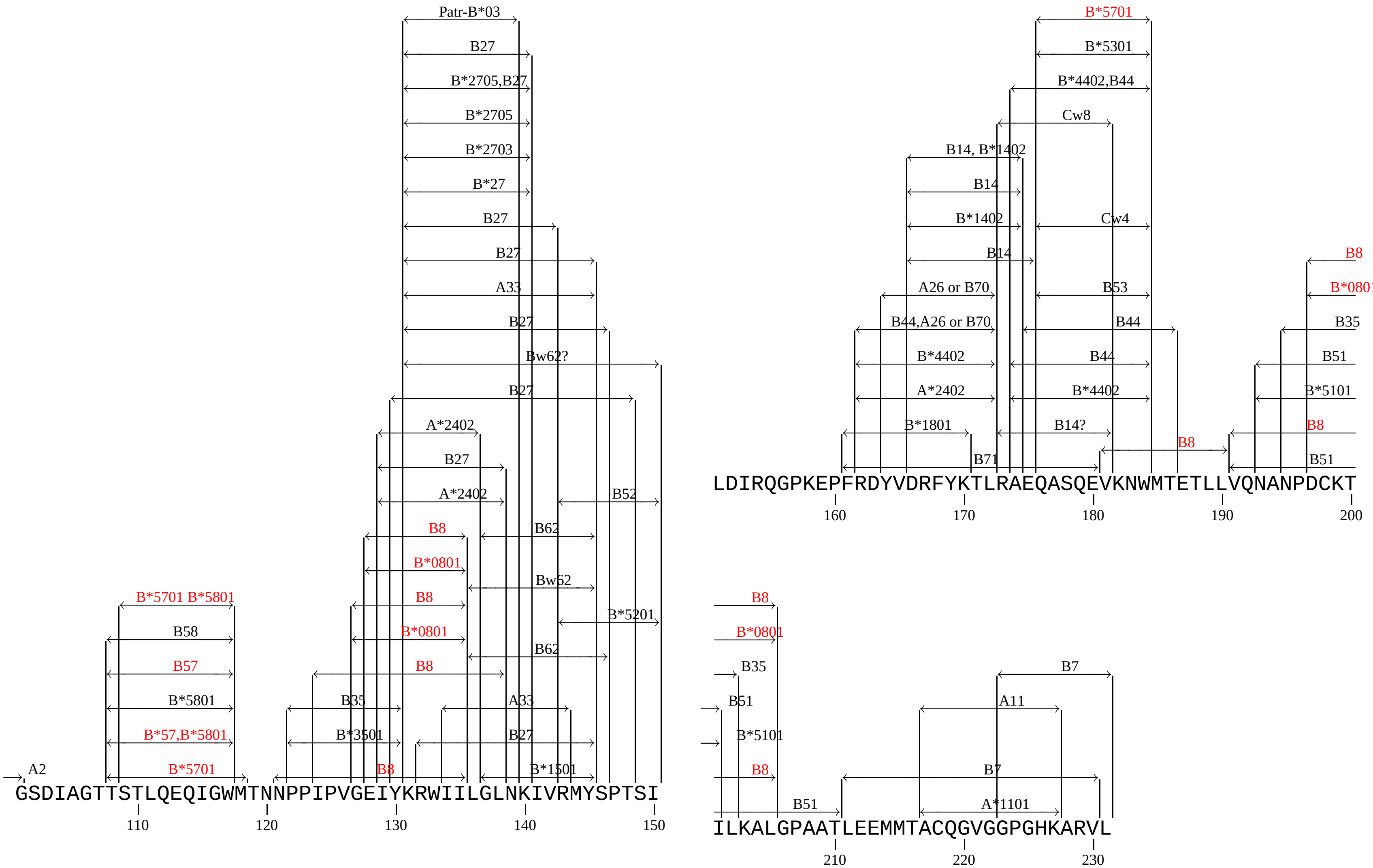
60
70
80
90
100


Patr-B*03
B27
B*2705,B27
B*2705
B*2703
B*27
B27
B27
A33
B27
Bw62?
B27
A*2402
B27
A*2402
B52
B8
B62
B*0801
Bw62
B*5701 B*5801
B8
B*5201
B58
B*0801
B62
B57
B8
B*5801
B35
A33
B*57,B*5801
B*3501
B27
A2
B*5701
B8
B*1501
GSDIAGTTSTLQEQIGWMTNNPPIPVGEIYKRWIILGLNKIVRMYSPTSI
110
120
130
140
150
B*5701
B*5301
B*4402,B44
Cw8
B14, B*1402
B14
B*1402
Cw4
B14
B8
A26 or B70
B53
B*0801
B44,A26 or B70
B44
B35
B*4402
B44
B51
A*2402
B*4402
B*5101
B*1801
B14?
B8
B8
B71
B51
LDIRQGPKEPFRDYVDRFYKTLRAEQASQEVKNWMTETLLVQNANPDCKT
160
170
180
190
200
B8
B*0801
B35
B7
B51
A11
B*5101
B8
B7
B51
A*1101
ILKALGPAATLEEMMTACQGVGGPGHKARVL
210
220
230

p2p7p1p6 CTL Map

AEAMSQVTNSATIMMQRGNFRNQRKIVKCFNCGKEGHTARNCRAPRKKGC

10 20 30 40 50

p2 <- start

p2 end <> p7 start

A2 A2

WKCGKEGHQMKDCTERQANFLGKIWPSYKGRPGNFLQSRPEPTAPPEESF

60 70 80 90 100

p7 end <> p1 start

p1 end <> p6 start

B7

RSGVETTTPPQKQEPIDKELYPLTSLRSLFGNDPSSQ

110 120 130

p6 end ->

Protease CTL Map

A*7401

A*6802,A*7401,A19

A*6802 A*6802

PQVTLWQRPLVTIKIGGQLKEALLDTGADDTVLEEMSLPGRWKPKMIGGI

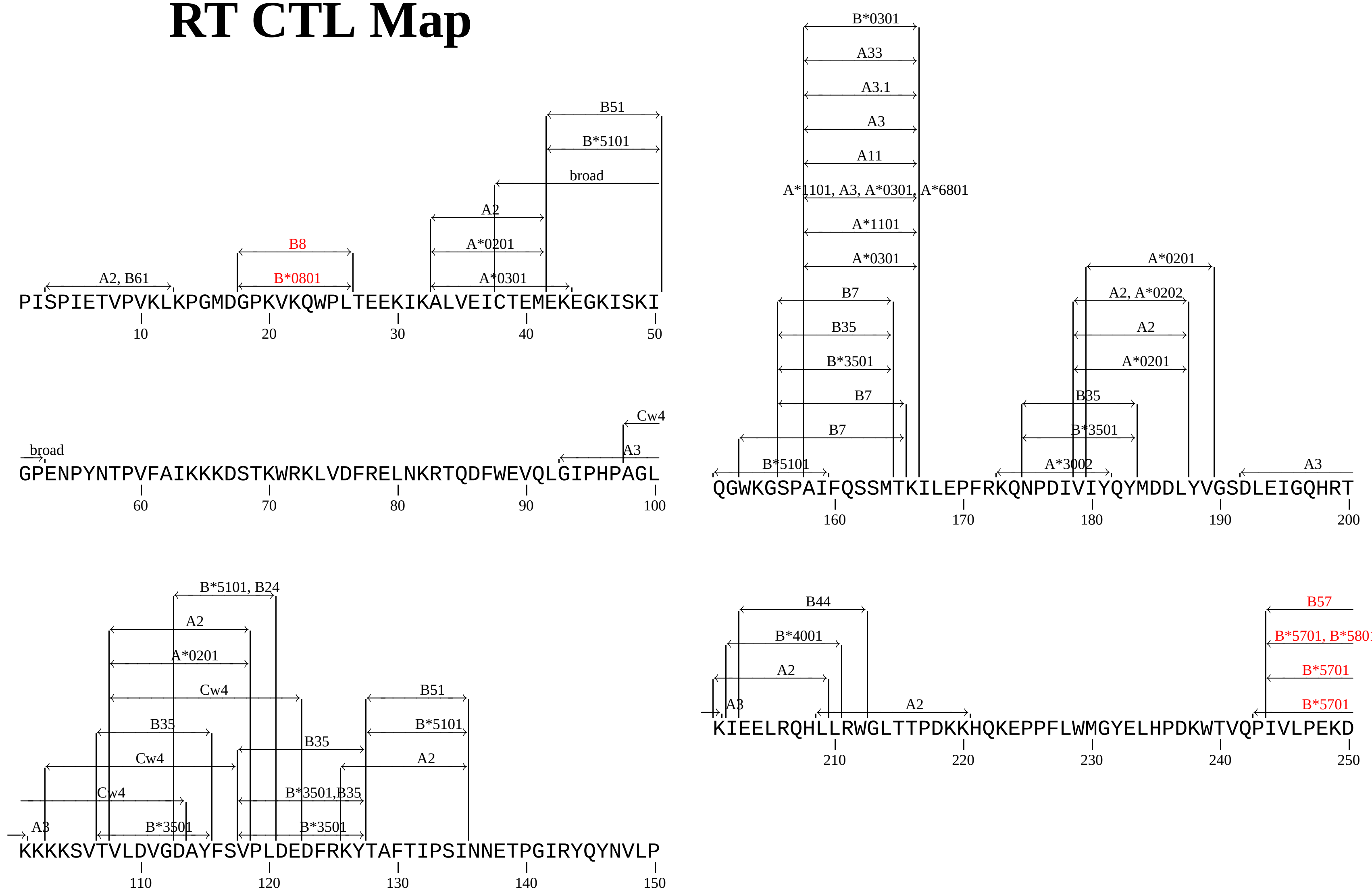
10 20 30 40 50

A*0201

GGFIKVRQYDQILIEICGHKAIGTVLVGPTPVNIIGRNLLTQIGCTLNF

60 70 80 90

RT CTL Map



B51
B*5101
broad
A2
A*0201
B8
B*0801
A*0301
A2, B61
PISPIETVPVKLKPGMDGPKVKQWPLTEEKIKALVEICTEMEKEGKISKI
10 20 30 40 50
Cw4
A3
broad
GPENPYNTPVFAIKKKDSTKWRKLVDFRELNKRTQDFWEVQLGIPHPAGL
60 70 80 90 100
B*5101, B24
A2
A*0201
Cw4
B51
B35
B*5101
B35
Cw4
A2
Cw4
B*3501,B35
A3
B*3501
B*3501
KKKKSVTVLDVGDAYFSVPLDEDFRKYTAFTIPSINNETPGIRYQYNVLP
110 120 130 140 150
B*0301
A33
A3.1
A3
A11
A*1101, A3, A*0301, A*6801
A*1101
A*0301
A*0201
B7
A2, A*0202
B35
A2
B*3501
A*0201
B7
B35
B7
B*3501
B*5101
A*3002
A3
QGWKGSPAIFQSSMTKILEPFRKQNPDIVIYQYMDDLYVGSDLEIGQHRT
160 170 180 190 200
B44
B57
B*4001
B*5701, B*5801
A2
B*5701
A3
A2
B*5701
KIEELRQHLLRWGLTTPDKKHQKEPPFLWMGYELHPDKWTVQPIVLPEKD
210 220 230 240 250

B42
B*4201,B42
B*4201
B*5701, B*5801
A3
B57
A*3002
B35, B51
B*5701
Bw62
B35
B*5701
B*1501
B*3501

SWTVNDIQKLVGKLNWASQIYPGIKVRQLCKLLRGTKALTEVIPLTEEAE

260 270 280 290 300

A26
A28
B45
A*6802
B35, B51
B35
B44
B*3501
A*3201
A2
B35
A29

WWTEYWQATWIPEWEFVNTPPLVKLWYQLEKEPIVGAETFYVDGAANRET

410 420 430 440 450

p15 RNase start <-

A2, A*0202
A2
A*0201
A*02
B35, B51
Bw62
B35
B*1501
A*1101
B*3501
A*0201
A11

LELAENREILKEPVHGVYYDPSKDLIAEIQKQGQGQWTYQIYQEPFKNLK

310 320 330 340 350

B14, B*1402
A2.1
A2
Cw8
A29
B14

KLGKAGYVTNRGRQKVVTLTDTTNQKTELQAIYLALQDSGLEVNIVTDSQ

460 470 480 490 500

B14, B*1402
Cw8
A*1101
B14
A2
B7

YALGIIQAQPDQSESELVNQIIEQLIKKEKVYLAWVPAHKGIGGNEQVDK

510 520 530 540 550

LVSAGIRKVL

-> p15 RNase end

B*5701 B*5801
B70
B*5701
B44
A11
A28, A*6802
A*3201

TGKYARMRGAHTNDVKQLTEAVQKITTESIVIWGKTPKFKLPIQKETWET

360 370 380 390 400

Integrase CTL Map

B*5101

FLDGIDKAQDEHEKYHSNWRAMASDFNLPPVVAKEIVASCDKCQLKGEAM

10 20 30 40 50

A*2402 A*6802

HGQVDCSPGIWQLDCTHLEGKVILVAVHVASGYIEAEVIPAETGQETAYF

60 70 80 90 100

A*6802

LLKLAGRWPVKTIHTDNGSNFTGATVRAACWWAGIKQEFGIPYNPQSQGV

110 120 130 140 150

A*1101

B57

B*5701

VESMNKELKKIIGQVRDQAEHLKTAVQMAVFIHNFKRKGGIGGYSAGERI

160 170 180 190 200

A2

A*0201

VDIIATDIQTKELQKQITKIQNFRVYYRDSRNPLWKGPAKLLWKGEGAVV

210 220 230 240 250

IQDNSDIKVVPRRKAKIIRDYGKQMAGDDCVASRQDED

260 270 280

Rev CTL Map

B*5801

B*5701

MAGRSGDSDEELIRTVRLIKLLYQSNPPPNPEGTRQARRNRRRRWRERQR

10 20 30 40 50

Cw5

B14, Cw8

A1 B14

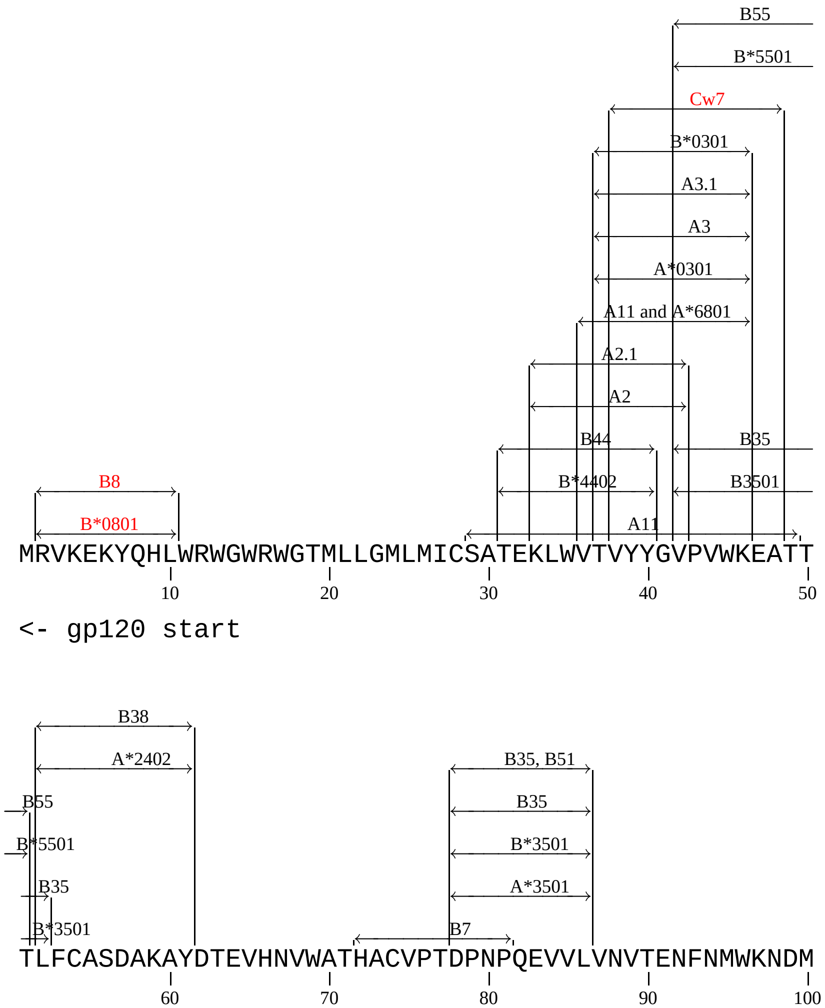
QIHSISERILGTYLGRSAEPVPLQLPPLERLTLDCNEDCGTSGTQGVGSP

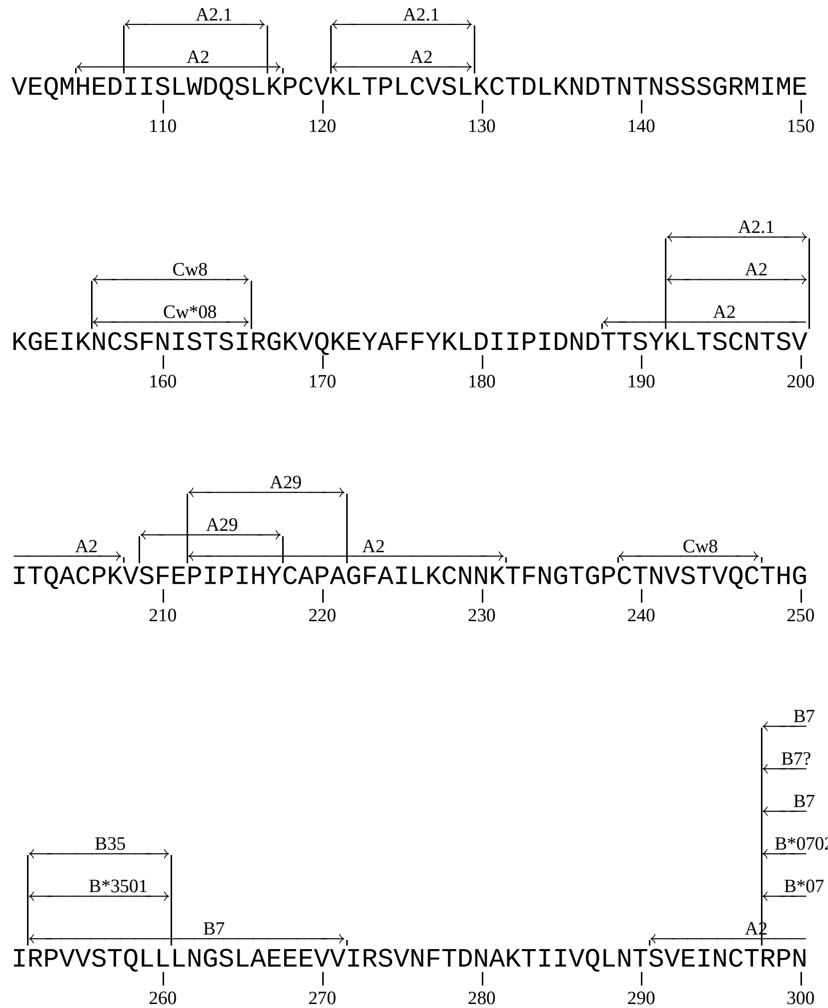
60 70 80 90 100

QILVESPTVLESGTKE

110

gp160 CTL Map





A*2402
A2, A3
A2
A11
B7
B7?
B7
B27
B*0702
H-2d
B*07
A2
Patr-B*14
A2
A*0201
CD4+ CTL

```
NNTRKRIRIQRGPGRAFVTIGKIGNMRQAHCNISRAKWNNTLKQIASKLR
```

310 320 330 340 350

A*2402
Cw4
A29
A2
Cw4
C*0401
B63,B15
B15
B*1516
CD4+ CTL
A2
A2

```
EQFGNNKTIIFKQSSGGDPEIVTHSFNCGGEFFYCNSTQLFNSTWFNSTW
```

360 370 380 390 400

A2
A2
A32
A29,A32
A*3201
B*5101
DR4 CD4+
A2
CD4+DRA
Mamu A*01

```
STEGSNNTEGSDTITLPCRIKQIINMWQKVGKAMYAPPISGQIRCSSNIT
```

410 420 430 440 450

A2

```
GLLLTRDGGNSNNESEIFRPGGGDMRDNWRSELYKYKVVKIEPLGVAPTK
```

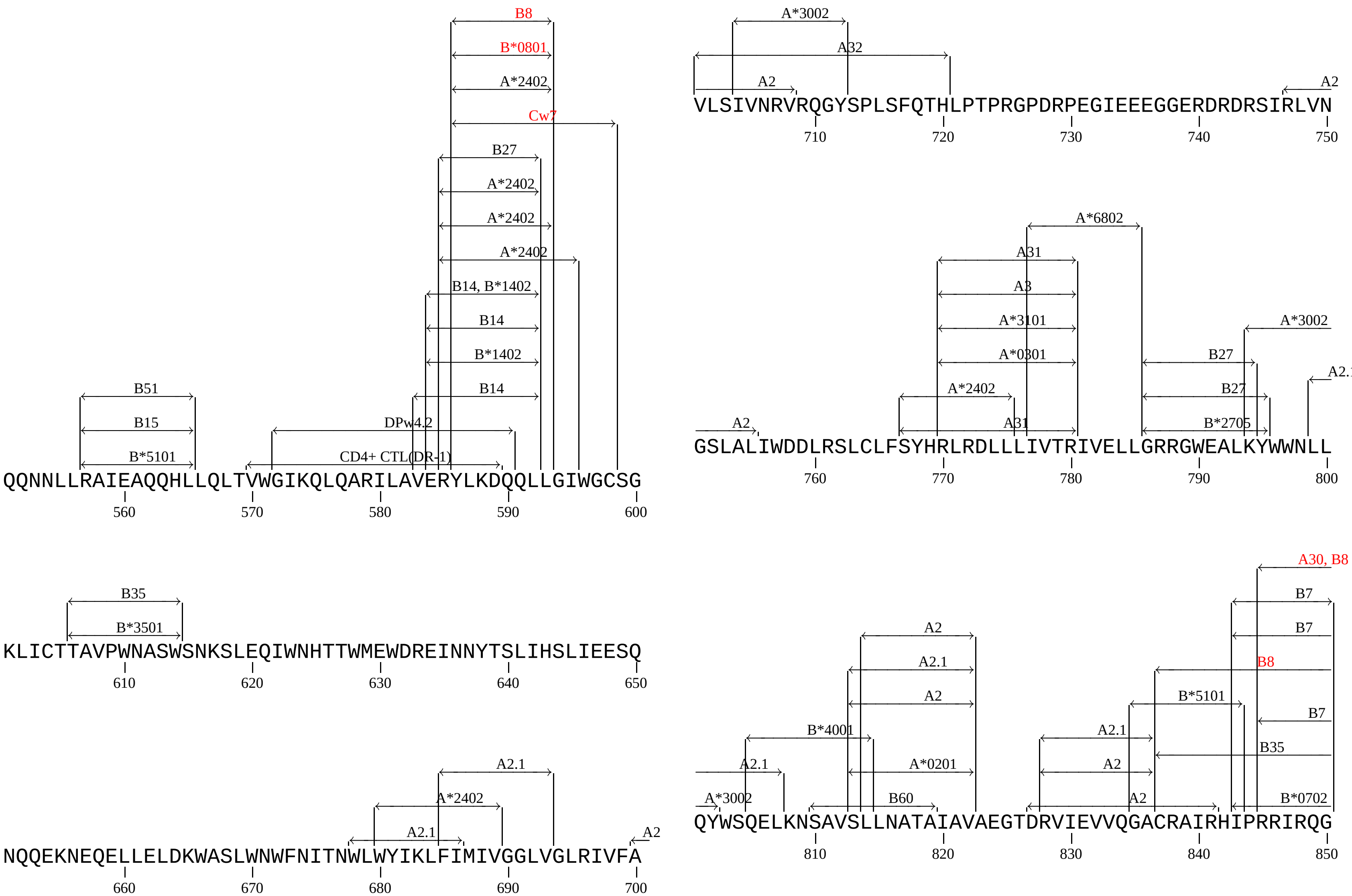
460 470 480 490 500

A2

```
AKRRVVQREKRAVGIGALFLGFLGAAGSTMGAASMTLTVQARQLLSGIVQ
```

510 520 530 540 550

gp120 end <> gp41 start

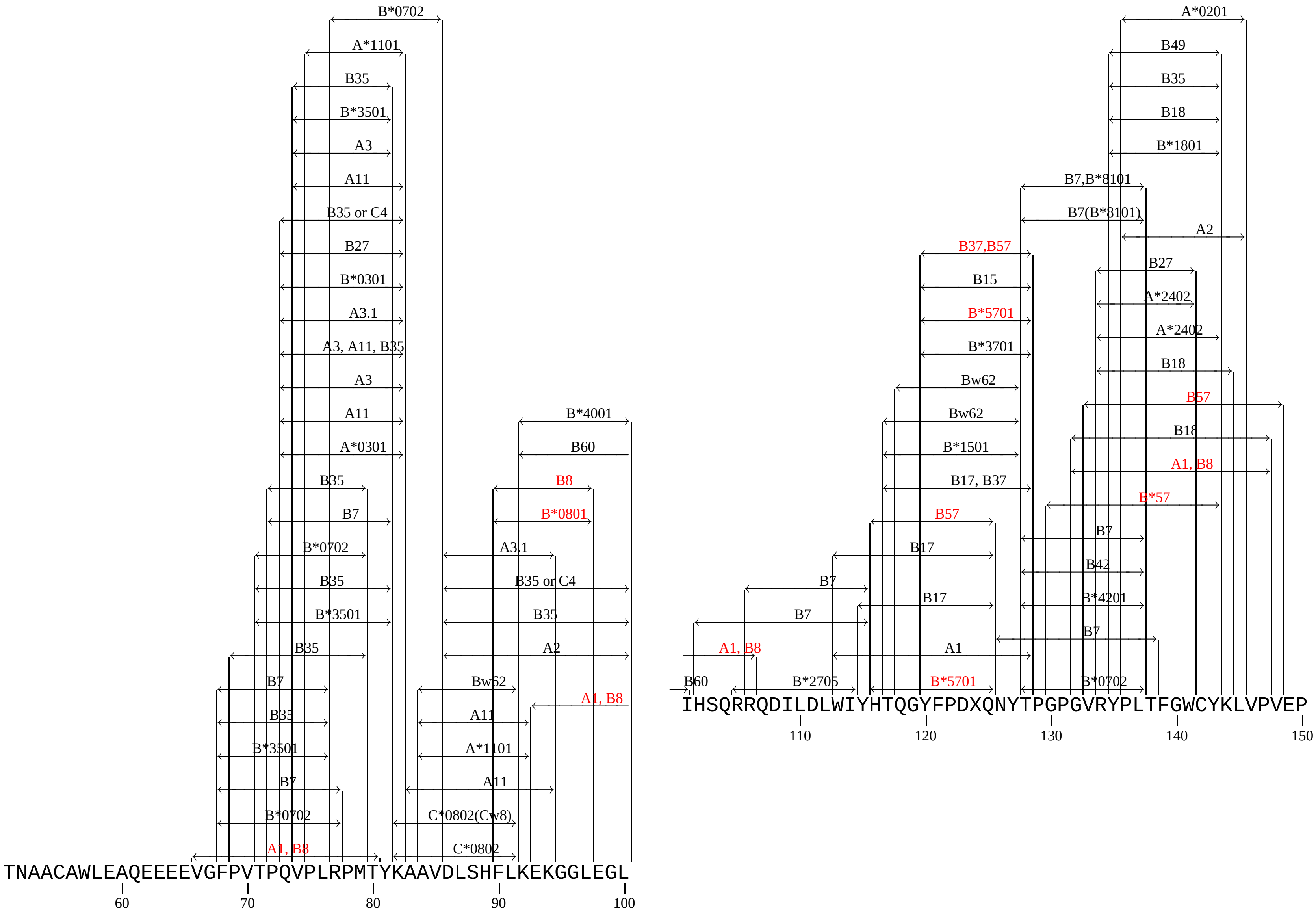

B8
B*0801
A*2402
Cw7
B27
A*2402
A*2402
A*2402
B14, B*1402
B14
B*1402
B14
B51
B15
B*5101
DPw4.2
CD4+ CTL(DR-1)
QQNNLLRAIEAQQHLLQLTVWGIKQLQARILAVERYLKDQQLLGIWGCSG
560 570 580 590 600
B35
B*3501
KLICTTAVPWNASWSNKSLEQIWNHTTWMEWDREINNYTSLIHSLIEESQ
610 620 630 640 650
A2.1
A*2402
A2.1
A2
NQQEKNEQELLELDKWASLWNWFNITNWLWYIKLFIMIVGGLVGLRIVFA
660 670 680 690 700
A*3002
A32
A2
A2
VLSIVNRVRQGYSPLSFQTHLPTPRGPDRPEGIEEEGGERDRDRSIRLVN
710 720 730 740 750
A*6802
A31
A3
A*3101
A*3002
A*0301
B27
A2.1
A*2402
B27
A2
A31
B*2705
GSLALIWDDLRSLCLFSYHRLRDLLLIVTRIVELLGRRGWEALKYWWNLL
760 770 780 790 800
A30, B8
B7
A2
B7
A2.1
B8
A2
B*5101
B*4001
A2.1
B7
B35
A2.1
A*0201
A2
A*3002
B60
A2
B*0702
QYWSQELKNSAVSLLNATAIAVAEGTDRVIEVVQGACRAIRHIPRRIRQG
810 820 830 840 850

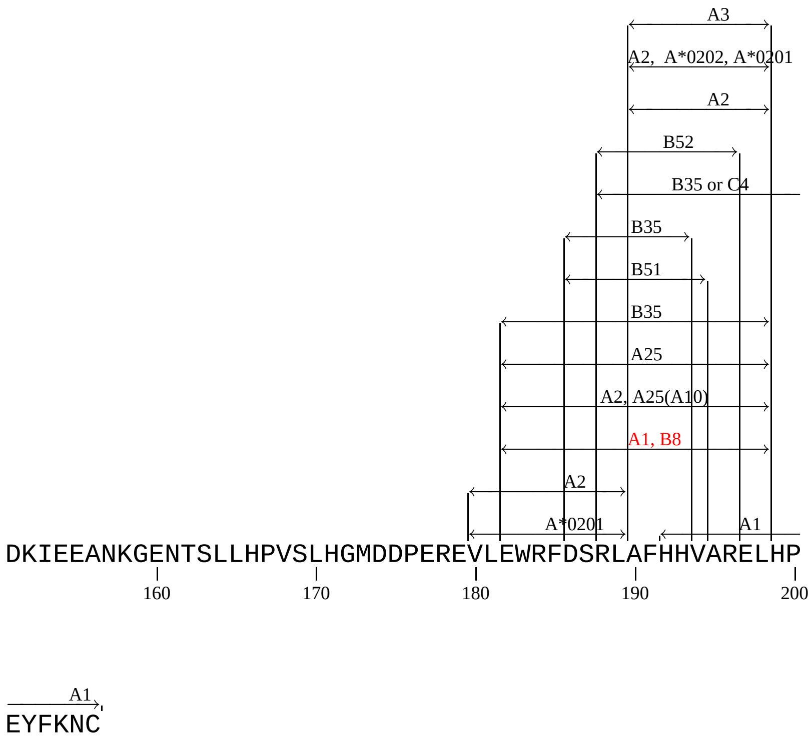
B7
A30, B8
B7
B*0702
B8
B35
LERILL

-> gp41 end

Nef CTL Map

B8
B*0801
MGGKWSKSSVIGWPTVRERMRRAEPAADRVGAASRDLEKHGAITSSNTAA
10 20 30 40 50


B*0702
A*1101
B35
B*3501
A3
A11
B35 or C4
B27
B*0301
A3.1
A3, A11, B35
A3
A11
A*0301
B35
B7
B*0702
B35
B*3501
B35
B7
B35
B*3501
B7
B*0702
A1, B8
B*4001
B60
B8
B*0801
A3.1
B35 or C4
B35
A2
Bw62
A1, B8
A11
A*1101
A11
C*0802(Cw8)
C*0802
TNAACAWLEAQEEEEVGFPVTPQVPLRPMTYKAAVDLSHFLKEKGGLEGL
60
70
80
90
100
A*0201
B49
B35
B18
B*1801
B7,B*8101
B7(B*8101)
A2
B37,B57
B27
B15
A*2402
B*5701
A*2402
B*3701
B18
Bw62
B57
Bw62
B18
B*1501
A1, B8
B17, B37
B*57
B57
B7
B17
B42
B7
B17
B*4201
B7
B7
A1, B8
A1
B60
B*2705
B*5701
B*0702
IHSQRRQDILDLWIYHTQGYFPDXQNYTPGPGVRYPLTFGWCYKLVPVEP
110
120
130
140
150



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[Price (1997)] D. A. Price, P. J. Goulder, P. Klenerman, A. K. Sewell, P. J. Easterbrook, M. Troop, C. R. Bangham, & R. E. Phillips. Positive selection of HIV-1 cytotoxic T lymphocyte escape variants during primary infection. *Proc Natl Acad Sci USA* **94**:1890–5, 1997. (Medline: 97203157) Notes: Cytotoxic T lymphocytes (CTLs) are thought to play a crucial role in the termination of the acute primary HIV-1 syndrome, but clear evidence for this presumption has been lacking. Here we demonstrate positive selection of HIV-1 proviral sequences encoding variants within a CTL epitope in Nef, a gene product critical for viral pathogenicity, during and after seroconversion. These positively selected HIV-1 variants carried epitope sequence changes that either diminished or escaped CTL recognition. Other proviruses had mutations that abolished the Nef epitope altogether. These results provide clear evidence that CTLs exert selection pressure on the viral population in acute HIV-1 infection.

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[Sipsas (1997)] N. V. Sipsas, S. A. Kalams, A. Trocha, S. He, W. A. Blattner, B. D. Walker, & R. P. Johnson. Identi£cation of type-speci£c cytotoxic T lymphocyte responses to homologous viral proteins in laboratory workers accidentally infected with HIV-1. *J Clin Invest* **99**:752–62, 1997. (Medline: 97197584) Notes: To examine a situation where the autologous strain and the reference reagents would be the same, the CTL response of three lab workers accidentally infected with HIV IIIB was studied. Both group speci£c and type speci£c epitopes were targets for CTL clones. One subject had a broadening of CTL response over time, using a broad range of restricting HLA class I alleles. Characterization of the cytotoxic T lymphocyte (CTL) response against HIV-1 has been limited by the use of target cells expressing viral proteins from laboratory isolates of HIV-1. This approach has favored identi£cation of group-speci£c CTL responses and precluded assessment of the extent of type-speci£c CTL responses directed against HIV-1. Using cells expressing viral proteins from the HIV-1 IIIB strain, we performed a detailed characterization of HIV-1-speci£c CTL response in three laboratory workers accidentally infected with HIV-1 IIIB. Eight of the epitopes identi£ed were group speci£c, lying in relatively conserved regions of Gag, reverse transcriptase, and envelope. Three type-speci£c epitopes were identi£ed, two of them in highly variable regions of envelope. In longitudinal studies in one subject, seven different epitopes and £ve different restricting HLA class I alleles were identi£ed, with a progressive increase in the number of CTL epitopes recognized by this subject over time. Our data demonstrate that type-speci£c CTL responses make up a signi£cant proportion of the host cellular immune response against HIV-1 and that a broadening of epitope speci£city may occur.

[Sutton (1993)] J. Sutton, S. Rowland-Jones, W. Rosenberg, D. Nixon, F. Gotch, X.-M. Gao, N. Murray, A. Spoonas, P. Driscoll, M. Smith, A. Willis, & A. McMichael. A sequence pattern for peptides presented to cytotoxic T lymphocytes by HLA B8 revealed by analysis of epitopes and eluted peptides. *Eur J Immunol* **23**:447–453, 1993. (Medline: 93170395).

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[Weekes (1999b)] M. P. Weekes, M. R. Wills, K. Mynard, R. Hicks, J. G. Sissons, & A. J. Carmichael. Large clonal expansions of human virus-speci£c memory cytotoxic T lymphocytes within the CD57+ CD28- CD8+ T cell population. *Immunology* **98**:443–9, 1999b. (Medline: 20051328).